REMARKS

The Office Action of July 23, 2002, has been carefully reviewed. Claims 29-36 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claim 29 has been objected to for using (I) and (ii) as they should be consistent. Appropriate correction to claim 29 is made thereby obviating this objection.

Claims 29-32 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, and 4 of U.S. Patent 6,207,641 B1 in view of U.S. Patent No. 4,588,535, U.S. Patent 5,776,731, or U.S. Patent 6,156,301.

This rejection is obviated by the terminal disclaimer attached hereto.

Claims 29-32 have been rejected under 35 U.S.C. §103(a) as being obvious over claims 1, 3, and 4 of U.S. Patent 6,207,641 B1 in view of U.S. Patent 4,588,585, U.S. Patent 5,776,731, or U.S. Patent 6,156,301. The examiner indicated that based upon an earlier effective U.S. filing date of the U.S. Patent 6,207,641 reference, it constitutes prior art under 35 U.S.C. §102(e).

The refiling of this application as a CPA effectively makes the instant application an application filed on or after November 29, 1999. Pursuant to 35 U.S.C. §103(c), subject matter developed by another person which qualifies as prior art only

under one or more subsections (e), (f), and (g) of section 102 shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, subject to an obligation of assignment to the same person or entity. The assignee of record in the instant application is the same Kabushiki Kaisha Hayashibara Seibutsu Kagaku Kenkyujo that is the assignee of record in U.S. Patent 6,207,641. At the time the invention was made, the subject matter of U.S. Patent 6,207,641 and of the presently claimed invention was subject to an obligation of assignment to Kabushiki Kaisha Hayashibara Seibutsu Kagaku Kenkyujo. Accordingly, this rejection is obviated by the filing of a CPA after November 29, 1999.

Claims 29-32 have been further provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 29, 33, 37, and 38 of copending application 08/982,285, now issued as U.S. Patent 6,476,197, which has an earlier filing date.

This rejection is also obviated by the terminal disclaimer attached hereto.

Claims 29-32 have been provisionally rejected under 35 U.S.C. §102(e) as being anticipated by copending application no. 08/982,285, now issued as U.S. Patent 6,476,197, which has a common inventor and assignee with the instant application. This rejection is respectfully traversed.

A postcard receipt for priority document(s), date-stamped April 30, 1998 by the USPTO, and a copy of a verified/certified English language translation of priority document JP 55468/1997, filed February 25, 1997, also date-stamped April 30, 1998 by the USPTO and made of record in the file (the USPTO sent back a copy of this English translation stamped "Applicant Copy") are attached hereto to show that the claim for foreign priority is now perfected by a certified copy of the priority document and a verified/certified English language translation thereof, both of which are of record in the file. The perfected priority filing date of February 25, 1997, antedates the December 1, 1997 filing date (102(e) date) of U.S. Patent 6,476,197 and overcomes the rejection based on §102(e) pursuant to MPEP 706.02(b). Accordingly, U.S. Patent 6,476,197 is not available as prior art against the present claims.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 29-32 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite because the examiner states that claim 29 recites "optionally" and it is unclear whether any of the limitations which follow the term "optionally" are required limitations. This rejection is respectfully traversed.

The recitation of "optionally" merely provides for alternate embodiments in which the limitation is either a required feature or a feature that is absent. This is clarified

by the addition of new claims 35 and 36 (dependent from claim 29) which positively recite the presence or absence of the "optional" feature in claim 29. Thus, the term "optionally" to be inclusive of two different embodiments is not indefinite.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 29-32 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Ushio et al., EP0712931 A2 or Okamura et al., U.S. Patent 5,912,324 and further in view of Mark et al., U.S. Patent 4,588,585. This rejection is respectfully traversed.

Mark merely teaches that, in connection with a specific protein, such as IL-2 and IFN-β, biological activity of a protein can be reserved stably even if cysteine residues that are not involved in disulfide linkage have been deleted or replaced with other amino acids. On the other hand, Ushio and Okamura disclose only the number and the position of cysteine residues in the amino acid sequence of IL-18. Based on these teachings and disclosures, it would have been difficult even for a skilled person to reasonably predict 1) which pairs of cysteine residues form a disulfide linkage between which is distinct from IL-2 or IFN-β, and 2) whether an IL-18 in which one or more cysteine residues are replaced with other amino acid residues would maintain its biological activity.

It is only the applicants who have found for the first time that active IL-18 contains no disulfide linkage and that the

biological activity of IL-18 can be maintained by replacing one or more cysteine residues with other amino acid residues so that disulfide linkage may not be formed or may be difficult to be formed in a molecule. Taking the variety of function and structure of proteins into account, it would have been difficult for one of ordinary skill in the art to apply the teachings of Mark with regard to IL-2 and IFN-β to other proteins, in particular IL-18, with a reasonable expectation of success.

In view of the above, the present claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claim 29 have been amended as follows:

29(Amended). An osteoclastgenic inhibitory composition for treating osteoclast-related diseases in a warm-blooded animal in need thereof, which comprises a pharmaceutically-acceptable carrier and, as an effective ingredient, an effective amount of (~~i~~i) an interleukin-18 comprising the amino acid sequence of SEQ ID NO:6 and a functional equivalent of said interleukin-18, or (ii) said functional equivalent, wherein said functional equivalent is capable of exerting osteoclastgenic inhibitory activity and comprises the amino acid sequence of SEQ ID NO:6, where one or more cysteine residues are replaced with a different amino acid residue(s) and optionally one or more amino acid residues are ~~added to~~inserted into the amino acid sequence of SEQ ID NO:6, or one or more amino acid residues in the amino acid sequence of SEQ ID NO:6 are additionally removed and/or replaced with other amino acid residue(s) but ~~having~~still retaining the amino acid sequences of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:4 ~~as consensus partial amino acid sequences in SEQ ID NOs: 6 and 7~~.